

AMENDMENTS TO THE CLAIMS:

Pursuant to 37 C.F.R. § 1.121, the following listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-258. (Canceled)

259. (Currently Amended) An isolated or recombinant polypeptide comprising an extracellular domain, said extracellular domain comprising an amino acid sequence having at least **about 91%** sequence identity to a subsequence of the polypeptide sequence set forth in SEQ ID NO:66, wherein the subsequence is the extracellular domain of SEQ ID NO:66, and wherein the isolated or recombinant polypeptide has a human CD28/human CTLA-4 binding affinity ratio **about** equal to or greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1 when **said isolated or recombinant polypeptide is expressed on a cell or bound to a cell membrane.**

260. (Previously Presented) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide is expressed on a cell or bound to a cell membrane.

261. (Currently Amended) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises an extracellular domain which comprises an amino acid sequence having at least **about 95%** sequence identity to the extracellular domain of SEQ ID NO:66, wherein said extracellular domain of SEQ ID NO:66 comprises at least amino acid residues 35-244 of SEQ ID NO:66.

262. (Currently Amended) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises an extracellular domain which comprises an amino acid sequence having at least **about 95%** sequence identity to the extracellular domain of SEQ ID NO:66, wherein the extracellular domain of SEQ ID NO:66 comprises at least amino acid residues 35-245 of SEQ ID NO:66.

263. (Previously Presented) The isolated or recombinant polypeptide of claim 261, wherein the polypeptide comprises an extracellular domain comprising at least amino acid residues 35-244 of SEQ ID NO:66.

264. (Canceled)

265 264. (Previously Presented) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide further comprises a signal peptide.

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~~266~~ ~~265.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 264, wherein the signal peptide comprises an amino acid sequence that has at least ~~about~~ 90% sequence identity to the amino acid sequence comprising residues 1-34 of SEQ ID NO:66.

~~267~~ ~~266.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 264, wherein the signal peptide has an amino acid sequence comprising amino acid residues 1-34 of SEQ ID NO:66.

~~268~~ ~~267.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises a transmembrane domain.

~~269~~ ~~268.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 267, wherein the polypeptide comprises the transmembrane domain of SEQ ID NO:66.

~~270~~ ~~269.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 268, wherein the transmembrane domain comprises an amino acid sequence having at least ~~about~~ 90% sequence identity to an amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

~~271~~ ~~270.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 269, wherein the transmembrane domain comprises an amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

~~272~~ ~~271.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide further comprises a cytoplasmic domain.

~~273~~ ~~272.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 271, wherein the polypeptide comprises the cytoplasmic domain of SEQ ID NO:66.

~~274~~ ~~273.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 271, wherein the cytoplasmic domain comprises an amino acid sequence having at least ~~about~~ 90% sequence identity to an amino acid sequence comprising at least amino acid residues 269-303 or 273-303 of SEQ ID NO:66.

~~275~~ ~~274.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 273, wherein the cytoplasmic domain comprises an amino acid sequence comprising at least amino acid residues 269-303 or 273-303 of SEQ ID NO:66.

~~276~~ ~~275.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises an amino acid sequence having at least ~~about~~ 90% sequence identity to the amino acid sequence comprising a mature domain of SEQ ID NO:66.

~~277~~ ~~276.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 275, wherein the mature domain comprises amino acid residues 35-303 of SEQ ID NO:66.

~~278~~ ~~271.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide comprises an amino acid sequence having at least ~~about~~ 90% sequence identity to the amino acid sequence corresponding to the signal peptide, extracellular domain and transmembrane domain of SEQ ID NO:66 which comprises at least amino acid residues 1-268 or 1-272 of SEQ ID NO:66.

~~279~~ ~~278.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has at least ~~about~~ 91% sequence identity to the full length amino acid sequence of SEQ ID NO:66.

~~280~~ ~~279.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 278, wherein the polypeptide comprises the full length amino acid sequence of SEQ ID NO:66.

~~281~~ ~~280.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has a human CD28/human CTLA-4 binding affinity ratio greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1.

~~282~~ ~~281.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has a binding affinity for CD28 that is ~~at least about equal to or~~ greater than the binding affinity of human B7-1 for CD28.

~~283~~ ~~282.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has a binding affinity for CTLA-4 that is less than the binding affinity of human B7-1 for CTLA-4.

~~284~~ ~~283.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 259, wherein the polypeptide has an ability to induce a T-cell proliferation response ~~about~~ equal to or greater than the T-cell proliferation response induced by human B7-1.

~~285~~ ~~284.~~ (Currently Amended) An isolated or recombinant polypeptide comprising an extracellular domain, said extracellular domain comprising an amino acid sequence having at least ~~about~~ 91% sequence identity to a subsequence of SEQ ID NO:66, said subsequence comprising at least amino acid residues 35-244 or 35-245 of SEQ ID NO:66, wherein said polypeptide induces a T-cell proliferation response ~~about~~ equal to or greater than the T-cell proliferation response induced by human B7-1 when said polypeptide is expressed on a cell or bound to a cell membrane.

~~286~~ ~~285.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 284, wherein the extracellular domain of said polypeptide comprises an amino acid sequence having at least 95% sequence identity to the subsequence of SEQ ID NO:66 that comprises at least amino acid residues 35-244 35-245 of SEQ ID NO:66.

~~287~~ ~~286.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 284, wherein the polypeptide comprises one or more of a signal peptide, transmembrane domain, and cytoplasmic domain.

~~288~~ ~~287.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 286, wherein the polypeptide comprises an amino acid sequence having at least ~~about~~ 95% sequence identity to the full length amino acid sequence of SEQ ID NO:66.

~~289~~ ~~288.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 259, wherein the cell is an antigen-presenting cell.

~~290~~ ~~289.~~ (Previously Presented) The polypeptide of claim 259, comprising at least one modified amino acid.

~~291~~ ~~290.~~ (Currently Amended) The polypeptide of claim ~~289~~ ~~288~~, wherein the modified amino acid is selected from: a glycosylated amino acid, a PEGylated amino acid, a farnesylated amino acid, an acetylated amino acid, a biotinylated amino acid, an amino acid conjugated to a lipid moiety, and an amino acid conjugated to an organic derivatizing agent.

~~292~~ ~~291.~~ (Currently Amended) An isolated or recombinant polypeptide comprising an amino acid sequence according to the formula:

MGHTM-X6-W-X8-SLPPK-X14-PCL-X18-X19-X20-QLLVLT-X27-LFYFCSGITPKSVTKRVKETVMLSCDY-X55-TSTE-X60-LTSLRIYW-X69-KDSKMVLAILPGKVQVWPEYKNRTITDMNDN-X101-RIVI-X106-ALR-X110-SD-X113-GTYTCV-X120-QKP-X124-LKGAYKLEHL-X135-SVRLMIRADFPVP-X149-X150-X151-DLGNPSPNIRRLLICS-X167-X168-X169-GFPRPHL-X177-WLENGEELNATNTT-X192-SQDP-X197-T-X199-LYMISSEL-X208-FNVTNN-X215-SI-X218-CLIKYGEL-X227-VSQIFPWWSKPKQEPPIDQLPF-X249-VIIPVSGALVL-X261-A-X263-VLY-X267-X268-ACRH-X273-ARWKRTTRNEETVGTE RLSPIYLGSAQSSG (SEQ ID NO:284), or an extracellular domain subsequence thereof comprising amino acid residues at positions 35-244,

wherein the amino acid residue at position X6 is Lys or Glu; position X8 is Arg or Gly; position X14 is Arg or Cys; position X18 is Trp or Arg; position X19 is Pro or Leu; position

X20 is Ser or Pro; position X27 is Asp or Gly; position X55 is Asn or Ser; position X60 is Glu or Lys; position X69 is Gln or Arg; position X101 is Pro or Leu; position X106 is Leu or Gln; position X110 is Pro or Leu; position X113 is Lys or Ser; position X120 is Val or Ile; position X124 is Val or Asp; position X135 is Thr or Ala; position X149 is Thr, Ser, or deleted; position X150 is Ile or deleted; position X151 is Asn or Thr; position X167 is Thr or deleted; position X169 is Ser or deleted; position X169 is Gly or deleted; position X177 is Cys or Tyr; position X192 is Val or Leu; position X197 is Gly or Glu; position X199 is Glu or Lys; position X208 is Gly or Asp; position X215 is His or Arg; position X218 is Ala or Val; position X227 is Ser or Leu; position X249 is Trp, Leu, or Arg; position X261 is Ala or Thr; position X263 is Val, Ala, or Ile; position X267 is Arg or Cys; position X268 is Pro or Leu; and position X273 is Gly or Val, and

wherein the polypeptide has a human CD28/human CTLA-4 binding affinity ratio ~~about~~ equal to or greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1 and/or induces a T-cell proliferation or activation response when the isolated or recombinant polypeptide is expressed on a cell or bound to a cell membrane.

~~293~~ ~~292.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 291, wherein the polypeptide has a human CD28/human CTLA-4 binding affinity ratio ~~about~~ greater than the human CD28/human CTLA-4 binding affinity ratio of human B7-1.

~~294~~ ~~295.~~ (Currently Amended) The isolated or recombinant polypeptide of claim 291, wherein the polypeptide induces a T-cell proliferation response ~~about~~ equal to or greater than that induced by human B7-1.

~~295~~ ~~294.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 291, comprising three or more of: Lys at position X6; Arg at position X8; Arg at position X14; Trp at position X18; Pro at position X19; Ser at position X20; Asp at position X27; Asn at position X55; Leu at position X106; Pro at position X110; Lys at position X113; Val at position X120; Val at position X124; Thr at position X135; Asn at position X151; Cys at position X177; Val at position X192; Gly at position X197; Glu at position X199; Gly at position X208; His at position X215; Ala at position X218; Trp at position X249; Ala at position X261; Val at position X263; Arg at position X267; Pro at position X268; and Gly at position X273.

~~296~~ ~~295.~~ (Previously Presented) The isolated or recombinant polypeptide of claim 294, comprising three or more of: Arg at position X8; Arg at position X14; Trp at position X18; Pro at position X19; Ser at position X20; Pro at position X110; Val at position X120; Val at position X124;

Cys at position X177; Val at position X192; Gly at position X197; Glu at position X199; Gly at position X208; His at position X215; Ala at position X218; Trp at position X249; Ala at position X261; and Val at position X263.

297 296. (Previously Presented) The isolated or recombinant polypeptide of claim 295, comprising amino acid residues 35-244 of SEQ ID NO:66.

298 297. (Currently Amended) An isolated or recombinant polypeptide comprising an amino acid sequence having at least ~~about~~ 91% sequence identity to the complete amino acid sequence set forth in SEQ ID NO:66, wherein said polypeptide when expressed on a cell or bound to a cell membrane has a human CD28/human CTLA-4 binding affinity ratio at least ~~about~~ equal to the human CD28/human CTLA-4 binding affinity ratio of human B7-1 or induces a T-cell proliferation or activation response.

299 298. (Currently Amended) A pharmaceutical composition comprising a polypeptide of claim 259 and a pharmaceutically acceptable excipient.

300 299. (Previously Presented) An isolated or recombinant polypeptide comprising an amino acid sequence comprising at least amino acid residues 245-268 or 246-272 of SEQ ID NO:66.

301 300. (Previously Presented) An isolated or recombinant polypeptide comprising an amino acid sequence comprising at least amino acid residues 269-303 or 273-303 of SEQ ID NO:66.

302 301. (Previously Presented) The isolated or recombinant polypeptide of claim 264, wherein the polypeptide comprises an amino acid sequence comprising at least amino acid residues 1-244 or 1-245 of SEQ ID NO:66.

303-368 302-367. (Canceled)

369 368. (Previously Presented) A polypeptide which is specifically bound by a polyclonal antisera raised against the polypeptide of claim 259.

370-382 369-381. (Canceled)

383 382. (New) The isolated or recombinant polypeptide of claim 285, wherein said extracellular domain comprises an amino acid sequence having at least 97% sequence identity to the subsequence of SEQ ID NO:66 comprising at least amino acid residues 35-244.

384 383. (New) The isolated or recombinant polypeptide of claim 285, wherein said polypeptide when expressed on a cell or bound to a cell membrane induces a T-cell proliferation response greater than the T-cell proliferation response induced by human B7-1.

385 ~~384.~~ (New) The isolated or recombinant polypeptide of claim 297, wherein said polypeptide comprises an amino acid sequence having at least 95% sequence identity to the complete amino acid sequence of SEQ ID NO:66, and wherein said polypeptide when expressed on a cell or bound to a cell membrane has a human CD28/human CTLA-4 binding affinity ratio that is at least equal to the human CD28/CTLA-4 binding affinity ratio of human B7-1.

386 ~~385.~~ (New) The isolated or recombinant polypeptide of claim 384, wherein said polypeptide when expressed on a cell or bound to a cell membrane has a human CD28/human CTLA-4 binding affinity ratio that is greater than the human CD28/CTLA-4 binding affinity ratio of human B7-1.

387 ~~386.~~ (New) The isolated or recombinant polypeptide of claim 297, wherein said polypeptide comprises an amino acid sequence having at least 95% sequence identity to the complete amino acid sequence of SEQ ID NO:66, and wherein said polypeptide when expressed on a cell or bound to a cell membrane induces a T-cell proliferation or activation response.

388 ~~387.~~ (New) The isolated or recombinant polypeptide of claim 386, wherein said polypeptide comprises an amino acid sequence having at least 95% sequence identity to the complete amino acid sequence of SEQ ID NO:66, and wherein said polypeptide when expressed on a cell or bound to a cell membrane induces a T-cell proliferation or activation response.

389 ~~388.~~ (New) The isolated or recombinant polypeptide of claim 387, wherein said polypeptide when expressed on a cell or bound to a cell membrane induces a T-cell proliferation or activation response greater than that induced by human B7-1.

390 ~~389.~~ (New) A pharmaceutical composition comprising a polypeptide of claim 297 and a pharmaceutically acceptable excipient.

391 ~~390.~~ (New) A pharmaceutical composition comprising a polypeptide of claim 382 and a pharmaceutically acceptable excipient.

392 ~~391.~~ (New) A pharmaceutical composition comprising a polypeptide of claim 384 and a pharmaceutically acceptable excipient.

These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter.